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FIG.1

CCGGGTCGACCCACCGTCCGAAGGCCCCCTCACTCCGCTCCACTCCTCGGGCTGG
5 CTCTCCTGAGGATGCACCAGCGTACCCCCGGCAAGATGCCCTCCCTGTGTGGC
CGGAATCCTTGCTGTGGCTTCTCTGGCTGCTGGGGACCCCTCCATTCCAGCAGA
GTTGTCTCAGGCTTGGAGCCACAGGCCGTGTCTTACTTGAGCCCTGGTGTCCC
TTAAAAGGCCGCCCTCCTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCAGGG
CTGCAGGCCGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCGATGTCTTCA
10 GGCTCACCAAGGAGGACACAGAGCGCTATGTGCTACCAACCTAACATGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGCTCAGTTGGGTGCACCTGGTAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGTGGAGCCAGACCATCAACCTGAGGACGACACGGATCCTGCCATG
CTGACCTGGTCCTATATCACTAGGTTGACCTGGAGTTGCCTGATGTAACCGGCAG
15 GTGCGGGCGTCACCCAGCTGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA
CCGAGGACACTGGCTTCGACCTGGAGTCACCATTGCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCCGGCAGCGGCTGGGCCAGCGGACACGTGA
TGGCTTGGACGGCGCCGCCGCCCCGGCCTGCCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGCGCCTGGTGTGGACCCGCCGC
20 GGCCTCAACCCGGGTCGGCGGGCACCGCCGGATGCGCAGCCTGGCTACTACA
GCGCCAACGAGCAGTCGGCGCTGGCCTCGGCCAACAGGCTGCGCCTGCACCTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAAGCCCTCTCGTCCGCTCCCTGGATGGACAGAAATGTGGCGTGGAGA
AGTGGTGTCCAAGGGTCGCTGCCCTGGTGGAGCTGACCCCATAGCAGCAGT
25 GCATGGCGCTGGTAGCTGGGTCCTCGAAGTCCTGCTCCGCTCCTGCGGAGGA
GGTGTGGTACCAAGGAGGGCGAGTGCAACAACCCAGACCTGCCTTGGGGCGT
GCATGTGTTGGTGCCTGACCTCCAGGCCAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTATGTGCAACAGTCGCCAGGACCGACGCCAGCGCTGCGCTC
CTCCCCCTGGCGGCCCTCCTTCTACCACTGGGTGCTGTGTACACACAGCCAAGGG
30 GATGCTCTGTGCAAGACACATGTGCCGGCATTGGCAGAGAGCTTACATGAAGCGT
GAGACAGCTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCGGAGGACGGGA
CCCTGAGCCTGTGTGTGGCGACTGCAGGACATTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGGTGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTTTCACAGCTGGCAGAGCGAGAGAAATGTCACGTTCTGACAGT
35 TACCCCCAACCTGACCAAGTGTCTACATTGCCAACACAGGCCTCTTACACACTTGG
CGGTGAGGATGGAGGGCGCTATGCGTGGCTGGGAAGATGAGCATCTCCCTAACAC
CACCTACCCCTCCCTGGAGGATGGCGTGTGAGTACAGAGTGGCCCTACCGAG

Substituted

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GACCGGGCTGCCCGCCTGGAGGAGATCCGCATCTGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTACAGGCCTATGGCAGGGAGTATGGCAACCTCACCGCCAGACA
TCACCTCACCTACTTCCAGCCTAACGCCACGGCAGGCCTGGGTGTGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGCAGGGCTGCCTGGTAAACTACAGCTGCCTG
5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTCGCTGCTGAACCCCTGCCCTCCCTACTGGCGGTGGGA
GAATCAGGCCATGCAGCGCTCCTGTGGGGTGGCCTGCAGGGAGCCGGCAGTGC
TGCCTGGAGGCCAGGGCAGCCTCTGAAGACATTGCCCTCAGCCCAGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
10 AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGCAGATGCCCTGGAGGCTCCAGTGACTGAGG
GCCCTGGCTCCGTAGATGAGAACGCTGCCCTGCCCTGAGCCCTGTGTGGATGTCATG
TCCTCCAGGCTGGGCCATCTGGATGCCACCTCTGCAGGGAGAACGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGCTCAAGCTGCACACGTGTGGACCCCTGCCAGGG
15 TCGTGTCCGTCTCCTGCAGGGCAGGTCTGATGGAGCTGCCTTCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGCCCTGGCAAGCAAGCCTGGAG
CCGGCGGGAGGTCTGCCAGGCTGCCCTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGAGAGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTGGACACCCAGTGCCAGGGCT
20 GCCTGCCCGAACCCCCAGGAGGCCCTGCAGCCTGGAGGCCCTGCCACCTAGGTGGAA
AGTCATGTCCCTGGCCCATGTTGCCAGCTGTGCCCTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCCCTGT
GCCCGCTGGTGGGCCAGGCCAGTGTCCCCTGTCTATTGCCACTGCACCTACC
GCTGGCATGTTGCCACCTGGATGGAGTGCTCTGTTCTGTGGGATGGCATCCAGCG
25 CCGGCGTGACACCTGCCCTGGACCCAGGCCAGGCCCTGTGCCAGCTGATTCTGC
CAGCACTGCCCAAGCCGGTACTGTGCGTGGCTGCTGGCTGGCCCTGTGTGGAC
AGGGTACGCCAGCCTGGTCCCCACGAAGAACGCCCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTGAGCCAACAGGAACCATTGACAT
GCGAGGCCAGGGCAGGCAGACTGTGCAGTGGCATTGGCGGCCCTCGGGAGGT
30 GGTGACCCCTCCGCGTCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTCA
GCTCCAAGACCAACACGCTGGTGGTGGAGGCAGCGCTGCCGGCCAGGAGGTGGGG
TGCTGCTGCCGTATGGGAGGCCAGCTGCTCTGAAACCTCTACAGAGAATGTGACATG
CAGCTTTGGGCCCTGGGTGAAATCGTGAGCCCCCTCGCTGAGTCCAGCCACGAGTA
35 ATGCAGGGGGCTGCCGGCTTCAATTATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGCAGCAGGTGCTACTG

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GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCAGGGCCAGTACTGGACCCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

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FIG. 2

5

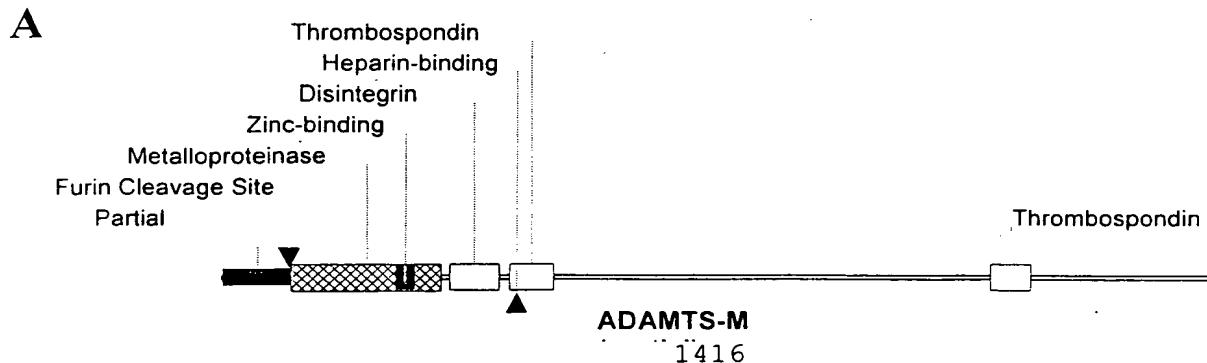
PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSGPAPLKRPPSPGFQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCWSQTINP
EDDTDPGHADLVLYITRFDELPGNRQVRGVQLGGACSPWSCLITEDTGFDLGVTIAHEI
10 GHSFGLHEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRQQLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLVPLLDGTECGVEKWCSPKGRCSRSLVELTPIAAVHGRWSSWGRSPCSRSCGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSCVS
15 GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAAGKMSISPNTTYSPLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEETYGNLTRPDITFTYFQPKPRQAWWWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPAWPEACVLEPCPPYWAvgDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQAQPAVALETCPQPCPARWEVSEPSCTSAGGAGLAL
20 ENETCVPGADGLEAPVTEGPGSVDEKLPAPPEPCVGMSCPPGWGHLDATSAKEKAPSPWG
SIRTGAQAAHWTPAAGSCSVSCGRGLMELRFLCMDSDLRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLPCPPRWKVMQLGPGSASCGLGTARRSVACVQLDQGQDVVEDEAACAAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRTCLGPQAQAPVPADFCQHLPKPVTVRGC
25 WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCABAIGR
PLGEVVTLRVLESSLNCAGDMLLWGRLTWRKMCRKLLDMTFSSKTNTLVRQRCGRPG
GGVLLRYGSQALAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

30

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Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) ADAMTS-M nucleotide sequence with translated amino acid sequence above.



B

```

+1 P G R P T R P K A P S H S A P L L G L A L L R M H Q R
                                         Partial Prodomain

=====
25 CCGGGTCGAC CCACCGCTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGACCCAGCG
GCCCGAGCTG GGTGCGCAGG CTTCCGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCG
=====
+1 H P R A R C P P L C V A G I L A C G F L L G C W G F
                                         Partial Prodomain

=====
105 TCACCCCCGG GCAAGATGCC CTCCCCCTCTG TGTGGCCGG AATCCTTGCT GTGGCTTCT CCTGGGCTGC TGGGGACCC
AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACCGA CACCGAAAGA GGACCCGACG ACCCCTGGGA
=====
+1 S H F Q Q S C L Q A L E P Q A V S S Y L S P G A P L K
                                         Partial Prodomain

=====
185 CCCATTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTAAAA
GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAAC CGGGACCAACG AGGGAATT
=====
+1 G R P P S P G F Q R Q R Q R R A A G G I L H L E L
                                         Furin Cleavage Site (Motif)
=====
                                         Partial Prodomain
                                         Metalloproteinase Domain
=====
265 GGCCGCCCTC CTTCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
CGGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA
=====
+1 L V A V G P D V F Q A H Q E D T E R Y V L T N L N I
                                         Metalloproteinase Domain
=====
345 GCTGGTGGCC GTGGGCCCG ATGTCTCCA GGCTCACCAAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
CGACCCACCGG CACCCGGGGC TACAGAAAGGT CCGAGTGGTC CTCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
=====
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+1 G A E L L R D P S L G A Q F R V H L V K M V I L T E P
Metalloproteinase Domain
=====

425 GGGCAGAACT GCTTCGGGAC CCGCCCTGG GGGCTCAGTT TCGGGTCAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1 E G A P N I T A N L T S S L L S V C G W S Q T I N P E
Metalloproteinase Domain
=====

505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCCTGA
CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

+1 D D T D P G H A D L V L Y I T R F D L E L P D G N R
Metalloproteinase Domain
=====

585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCTCTAT ATCACTAGGT TTGACCTGGA GTTGCCCTGAT GGTAACCCGGC
CCTGCTGTGC CTAGGACCCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

+1 Q V R G V T Q L G G A C S P T W S C L I T E D T G F D
Metalloproteinase Domain
=====

665 AGGTGCGGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCATTA CCGAGGACAC TGGCTTCGAC
TCCACGCCCG CCAGTGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCTGTG ACCGAAGCTG

+1 L G V T I A H E I G H S F G L E H D G A P G S G C G P
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCC
GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG

+1 S G H V M A S D G A A P R A G L A W S P C S R R Q L
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
GTCGCCTGTG CACTACCGAA GCCTGCCGCG CGCGGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCGTCGACG

+1 L S L L S A G R A R C V W D P P R P Q P G S A G H P P
Metalloproteinase Domain
=====

905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCCG GGTCCGCGGG GCACCCGCC
ACTCGGACGA GTCGCGTCCT GCCCGCGCGA CGCACACCCCT GGGCGGCCCG GGAGTTGGGC CCAGGCCGCC CGTGGCGGC

+1 D A Q P G L Y Y S A N E Q C R V A F G P K A V A C T F
Disintegrin Domain
=====

985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTGGCCCC AAGGCTGTGC CCTGCACCTT
CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA

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+1 A R E H L D M C Q A L S C H T D P L D Q S S C S R L
Disintegrin Domain

=====

1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCGG GCGACCTGGT TTCGTCGACG TCGGGAGGAG

+1 L V P L L D G T E C G V E K W C S K G R C R S L V E L
Disintegrin Domain

=====

1145 TCGTTCCCTC CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCCTC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTCCCAGCGA CGGCAGGGGA CCACCTCGAC

+1 T P I A A V H G R W S S W G P R S P C S R S C G G G V
Heparin-binding Motif

=====

1225 ACCCCCCATAG CAGCAGTGCA TGGGCCTGG TCTAGCTGGG GTCCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
TGGGGGTATC GTCGTACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCCTCCACA

+1 V T R R R Q C N N P R P A F G G R A C V G A D L Q A
Thrombospondin Submotif

=====

1305 GGTCAACCAGG AGGCAGGAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGGCG
CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

+1 E M C N T Q A C E K T Q L E F M S Q Q C A R T D G Q P
Thrombospondin Submotif

=====

1385 AGATGTGCAA CACTCAGGCC TGCAGAGAAGA CCCAGCTGGA GTTCATGTGCG CAACAGTGC CGAGGACCGA CGGCCAGCCG
TCTACACGT GTGAGTCCGG AGCCTCTCTC GGGTCGACCT CAAGTACAGC GTTGTACAGC GGTCTGGCT GCCGGTCCGG

+1 L R S S P G G A S F Y H W G A A V P H S Q G D A L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCA
GACGCGAGGA GGGGACCGCC GCGAGGAAG ATGGTACAGC CACGACGACA TGGTGTCGG GTCCTGGCT GCGGGTCCGG

+1 H M C R A I G E S F I M K R G D S F L D G T R C M P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
TGTGTACACG GCGCGGTAAAC CGCTCTCGA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATAACGGTT

+1 S G P R E D G T L S L C V S G S C R T F G C D G R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTCGG GGGCAGCTGC AGGACATTG GCTGTGATGG TAGGATGGAC
CACCGGGGGC CCTCCTGCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG

+1 S Q Q V W D R C Q V C G G D N S T C S P R K G S F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
AGGGTCTGTC ATACCCTGTC CACGGTCCAC ACACCACCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTG

+1 G R A R E Y V T F L T V T P N L T S V Y I A N H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
ACCGTCTCGC TCTCTTATAC AGTCAAAGA CTGTCATGG GGGTTGGACT GGTACAGAT GTAACGGTTG GTGTCCGGAG

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+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCTAA CACCACTAC
AGAAGTGTGT GAACGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGATT GTGGTGGATG

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E I R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGCGGACC TCCTCTAGGC

+1 I W G P L Q E D A D I Q V Y R R Y G E E Y G N L T R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGGGT ATGGCGAGGA GTATGGCAAC CTCACCGCC
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCCG

+1 P D I T F T Y F Q P K P R Q A W V W A A V R G P C S V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCTGGGTG TGGCCGCTG TGCGTGGGCC CTGCTGGTG
GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGGCCAC

+1 S C G A G L R W V N Y S C L D Q A R K E L V E T V Q C
2185 AGCTGTGGGG CAGGGCTGCG CTGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCAGTG
TCGACACCCCC GTCCCGACGC GACCCATTG ATGTCGACGG ACCTGGTCCG GTCCCTCCTC AACACACCTCT GACAGGTAC

+1 Q G S Q Q P P A W P E A C V L E P C P P Y W A V G D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGCG GTGGGAGACT
GGTCCCTCG GTCGTCGGTG GTCCGACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCCTCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A Q G S L L
2345 TCGGCCCATG CAGCGCCTCC TGTTGGGGTG GCCTGCGGGA CGGCCAGTG CGCTCGTGG AGGCCAGGG CAGCCTCTG
AGCCGGTAC GTCGCGAGG ACACCCCCAC CGGACCCCT CGCCGGTCAC GCGACGCACC TCCGGTCCC GTCGGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTGC CCCCAGCCCG GTGAGAGCA GGGGCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
TTCTGTAACG GGGTCCGGC CACGTCTCGT CCCCCGGTCG TCGGTGACA CGCGACCTT TGGACGTTGG GGGTCCGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGAGGTGT CAGAGCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCTTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGTC GAGTACGTGT AGTCGACCCAC CTCGTCCGGA CGCGACCTC TTGCTCTGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGAATGAGA GGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCTGAG
CACACGGTCC CGCTCTACCG GACCTCCGAG GTCACTGACT CCCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGATGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCTATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCGGGTAG ACCTACGGTG GAGACGTCCC CTCTCCGAG GGAGGGGTAC

+1 G. S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATC AGGACGGGGG CTCAGCTGC ACACGTGTGG ACCCCTGCCG CAGGGCTGTG CTCCGTCTCC TGCGGGCGAG
CCCCGTCTAG TCCTGCCCTCC GAGTCGACG TGTGCACACC TGGGGACGCC GTCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L M E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCACGGGA CAGGTCCCTC TCGACACACC GGACCGTTCG

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+1 K P G S R R E V C Q A V P C P A R W Q Y K L A A C S V
2905 AAGCCTGGGA GCCGGCGGGA GGTCGCCAG GCTGCTCCGT GCCCTGCTCG GTGGCAGTAC AAAGCTGGCGG CCTGCAGCGT
TTCGGACCCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTGACCGCC GGACGTCGCA

+1 S C G R G V V R R I L Y C A R A H G E D D G E E I L
2985 GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCCGGGCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
CTCGACACCC TCTCCCCAGC ACGCCTCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

+1 L D T Q C Q G L P R P E P Q E A C S L E P C P P R W K
3065 TGGACACCCA GTGCCAGGGG CTGCCCTGCC CGGAACCCCA GGAGGCCAGC AGCCTGGAGC CCTGCCACC TAGGTGGAAA
ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGT CCTCCGGACG TCGGACCTCG GGACGGGTGG ATCCACCTT

+1 V M S L G P C S A S C G L G T A R R S V A C V Q L D Q
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTGGTG GCTGTGTGC AGCTCGACCA
CACTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT

+1 G Q D V E V D E A A C A A L V R P E A S V P C L I A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGGCGGC CTGTGCGGGC CTGGTGGCGC CCGAGGCCAG TGTCCCCCTGT CTCATTGCCG
TCCGGTCCCTG CACCTCCACC TGCTCCGGC GACACGCCGC GACCACGGCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC

+1 D C T Y R W H V G T W M E C S V S C G D G I Q R R R D
Thrombospondin Submotif

=====
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTCC TGTGGGATG GCATCCAGCG CGGGCGTGAC
TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCGCGACTG

+1 T C L G P Q A Q A P V P A D F C Q H L P K P V T V R G
Thrombospondin Submotif

=====
3385 ACCTGCCTCG GACCCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
TGGACGGAGC CTGGGGTCCG GGTCCCGCGA CACGGTCAC TAAAGACGGT CGTAGGACGGG TTCGGCCACT GACACGCAAC

+1 C W A G P C V G Q G T P S L V P H E E A A A P G R T
Thrombospondin Submotif

=====
3465 CTGCTGGCT GGGCCCTGTG TGGGACAGGG TACGCCAGC CTGGTCCCC ACAGAAGAAC CGCTGCTCCA GGACGGACCA
GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTCG GCGACGAGGT CCTGCCTGGT

+1 T A T P A G A C G R Q H L E P T G T I D M R G P G Q A
3545 CAGCCACCCCG TGCTGGTGC TGTCAGGC AGCACCTGA GCCAACAGGA ACCATTGACA TGCGAGGCC AGGGCAGGCA
GTCGGTGGGG ACGACCACGG ACACCGTCG TCGTGGAACT CGGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCCTCCGGT

+1 D C A V A I G R P L G E V V T L R V L E S S L N C S A
3625 GACTGTGCAG TGGCCATTGG CGGGCCCCCTC GGGGAGGTGG TGACCCCTCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCAACG

+1 G D M L L L W G R L T W R K M C R K L L D M T F S S
3705 GGGGGACATG TTGCTGCTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCTGTACTGA AAGTCGAGGT

+1 K T N T L V V R Q R C G R P G G G V L L R Y G S Q L A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
TCTGGTTGTG CGACCACAC TCCGTCGCGA CGCCCGCCGG TCCTCCACCC CACGACGACG CCATACCTC GGTCGAACGA

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+1 P E T F Y R E C D M Q L F G P W G E I V S P S L S P A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTG GGCCCTGGGG TGAAATCGT AGCCCTCGC TGAGTCAGC
GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAC CCGGGACCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTG

+1 T S N A G G C R L F I N V A P H A R I A I H A L A T
3945 CACGAGTAAT GCAGGGGGCT GCGGCTCTT CATTATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
GTGCTCATTA CGTCCCCCGA CGGGCGAGAA GTAATTACAC CGAGGGGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

+1 N M G A G T E G A N A S Y I L I R D T H S L R T T A F
4025 ACATGGGCAGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
TGTACCCCGG ACCCTGGCTC CCTCGTTAC GGTGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

+1 H G Q Q V L Y W E S E S S Q A E M E F S E G F L K A Q
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTCAGC GAGGGCTTCC TGAAGGCTCA
GTACCCCGTCG TCCACGAGAT GACCCCTAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1 A S L R G Q Y W T L Q S W V P E M Q D P Q S W K G K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GTTAGTACC CATGGCCTCT ACGTCCCTGGG AGTCAGGACC TTCCCTTCC

+1 E G T
4265 AAGGAACC
TTCCCTTCC

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Fig. 4

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

		Percent Homology
		Sim Ident
		3.60
301		
hADAMTS-4 (AB014588)	(202) SPSPRR-----	RAKRESSLRF VETIVVZED KVAAGFG-AKRYLTVWAAA
hADAMTS-5 (AF142099)	(241) QSALSPAGGGPQIWWBRQ-----	44 32
hADAMTS-1 (AF060152)	(220) QGVQQTGTGSI-----	44 28
hADAMTS-8 (AF060153)	(199) ASEPPPIGAT-----	47 23
hADAMTS-2 (AJ003125)	(248) EHANSRR--R-----	47 29
M1-MPD	(1) -----	46 29
Consensus	P	49 32
361		
hADAMTS-4 (AB014588)	(251) KAFKHEPFRNPVSVNTRVLTGSGEEFQGP-----	420
hADAMTS-5 (AF142099)	(299) RTYSHATENHTRAWVAVVTKDKDKEVSK-----	
hADAMTS-1 (AF060152)	(274) RYKXHPTRNSVSEWVAVVTKDKDKEVSK-----	
hADAMTS-8 (AF060153)	(253) RYKXHEKNSAENLWVAVVTKDKDKEVSK-----	
hADAMTS-2 (AJ003125)	(300) EYKHDTEIGAHANVWVAVVTKDKDKEVSK-----	
M1-MPD	(39) EILRDEPQGAEVRLVYK-----	
Consensus	(361) RLYKHPSI N I LVVVK VIL D GPEV	480
421		
hADAMTS-4 (AB014588)	(310) I PDXQG QDGGS VSTEEDY MADIGIV D A-----	
hADAMTS-5 (AF142099)	(358) V AVDQG EDCGG HHSEEDY MADIGIV D A-----	
hADAMTS-1 (AF060152)	(333) V AVDQG QDGGS SODEDY MADIGIV D A-----	
hADAMTS-8 (AF060153)	(312) I TADQG QDGGS SODEDY MADIGIV D A-----	
hADAMTS-2 (AJ003125)	(360) I HADQG QDGGS SODEDY MADIGIV D A-----	
M1-MPD	(98) A LVIY YE F DDELPDNRQYR VEQGGASITW-----	
Consensus	(421) YDTAIIUFTRODLCG G CDTIGMADGT CDP RSC VIEEDGLQAFAT AHEIGHVLG	540
481		
hADAMTS-4 (AB014588)	(369) YL NSKPOISINELSTSRV AYMMHVPEED E SARFIDN DNGYGH E-----	
hADAMTS-5 (AF142099)	(417) IS DSKTGEETFSTE-DETI SSIITSIDASKE K TSATIHE DDEGDN E-----	
hADAMTS-1 (AF060152)	(392) VP DAKQGASTIN-VNODSM NSMISNLDSOP P SRYMILIS DNGCHG E-----	
hADAMTS-8 (AF060153)	(372) VP DSSPDTCTTFFPFG-KHMY ZAFLRVHAFRTH P SAVYIILIDGCHG DDEGAP-----	
hADAMTS-2 (AJ003125)	(416) YE SGG -- NRCDEVRLSHI ALVQQAHRTH P SQQEISRLIES-YD E-----	
M1-MPD	(158) YE GAP -- GEGCCESGG -- IV PESDGAAPAGLAA P SRRQILSEISAGRQW P-----	
Consensus	(481) M HDDSK C SL GP HVMAS D PWSPCSA LT FLD GHG CLD P	

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541
nADAMTS-4 (AB014588)
nADAMTS-5 (AF142099)
nADAMTS-1 (AF060132)
nADAMTS-8 (AF060153)
nADAMTS-2 (AJ003125)
M1-MPD
Consensus

(429) EAP--LH~~LP~~Y~~TE~~G--KDYADRCQLE~~EG~~DSR~~IC~~--QLPP~~PA~~ALW~~ES~~CHLN~~CH~~
(476) R~~K~~Q--ILG~~ED~~G--Q~~LD~~AT~~DN~~LE~~GE~~Y~~SV~~--GM~~D~~CAR~~LG~~AVR~~Q~~Q~~W~~
(451) QNP--I~~Q~~E~~SD~~PG--TS~~D~~DN~~RG~~OF~~EG~~DSK~~H~~C--DAA~~S~~TS~~TD~~IC~~TS~~SG~~YL~~
(431) GNA--LP~~U~~TC~~PG~~GR~~M~~AL~~Q~~D~~O~~OR~~Q~~LE~~G~~FR~~C~~HT~~S~~AO~~D~~Y~~V~~W~~CH~~TDGAEP~~IC~~
(471) FAD~~W~~PA~~L~~RP~~G~~--LH~~SM~~NE~~Q~~R~~F~~EG~~Y~~MM~~C~~TA~~F~~RT~~F~~DP~~Q~~W~~G~~CS--HPD~~N~~Y~~F~~
(213) RP

(541) A LP LPG YDA QC TFGPD HCP D CA LWC G C